Feasibility study protocol

Full title of trial	Cognitive Stimulation Therapy for people with Learning Disabilities and Dementia (CST-IDD). A mixed methods feasibility study.
Short title	CST-IDD
Version and date of protocol	Version 8 (1512/2021)
Sponsor:	North East London NHS Foundation Trust
Sponsor protocol number	
Funder (s):	NIHR-RfPB
ISRCTN / Clinicaltrials.gov no:	To be obtained once study is registered as a NIHR portfolio study
Intervention:	Group Cognitive Stimulation Therapy
Single site/multi-site:	Multi-site
Chief investigator (s):	**Sponsor Representative**:
Prof. Aimee Spector	Fiona Horton North East London NHS Foundation Trust R&D Department, Goodmayes Hospital Maggie Lillie Suite, Barley Lane Ilford, IG3 8XJ

Protocol Version History

Version Number	Date	Protocol Update Finalised By (insert name of person):	Reasons for Update
Version 1	23/04/2021	Elisa Aguirre	Feedback from study team
Version 2	05/05/2021	Elisa Aguirre	Updates from comments
Version 3	08/05/2021	Elisa Aguirre	Feedback from study zoom meeting
Version 4	07/09/2021	Elisa Aguirre	Inclusion of outcome measures ready for ethics application
Version 5	20/09/2021	Sarah Hoare	Updates from comments
Version 6	22/09/2021	Sarah Hoare	Feedback from study team and sponsor site.
Version 7	02/12/2021	Sarah Hoare	REC feedback
Version 8	15/12/2021	Sarah Hoare	Feedback from co-aplicants

Signatures

The Chief Investigator and NELFT have discussed this protocol. The investigator agrees to perform the investigations and to abide by this protocol.

The investigator agrees to conduct the trial in compliance with the approved protocol, the UK Data Protection Act (2018), the Trust Information Governance Policy (or other local equivalent), the current Research Governance Framework, the Sponsor's SOPs, and other regulatory requirements as amended.

Chief investigator(s)

Aimee Spector	Signature (s)	Date
Statistician		
Zoe Hoare	Signature (s) Signature	Date Date
Sponsor		
NELFT	Signature	Date

Contents

List of abbreviations

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CSRI	Client Service Receipt Inventory (resource use questionnaire)
CST	Cognitive Stimulation Therapy
EQ-5D-5L	EuroQol 5-dimension 5-level quality of life questionnaire
GAfREC	Governance Arrangements for NHS Research Ethics
GCP	Good Clinical Practice
HRA	Health Research Authority
LD	Learning Disability
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trial Number
NHS R&D	National Health Service Research & Development
NICE	National Institute of Health and Care Excellence
PI	Principal Investigator
PIS	Participant Information Sheet
PSSRU	Personal Social Services Research Unit
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
TMG	Trial Management Group

1 Trial personnel

See protocol cover page for Chief Investigator and Sponsor contact details.

CI: Prof Aimee Spector

e-mail: a.spector@ucl.ac.uk

Statistician: Dr Zoe Hoare
e-mail: z.hoare@bangor.ac.uk

Principal Investigatior NELFT: Prof. Afia Ali

Email:afia.ali@nelft.nhs.uk

Health Economist: Dr Caroline Clarke

Email: caroline.clarke@ucl.ac.uk

Qualitative researcher lead: Prof Georgina Charlesworth

Email: g.charlesworth@ucl.ac.uk

Research Assistant: Sarah Hoare

Email:s.hoare@nelft.nhs.uk

2 Summary

Objectives:	1. To assess the feasibility and acceptability of a randomised controlled trial of group CST for people with ID and dementia compared to Treatment as Usual. The results of this study will inform the design of a future definitive RCT.
Type of trial:	Feasibility randomised multi-site trial of group CST compared to "Treatment as usual" in participants with dementia and Learning disabilities.
Trial design and methods:	Fifty individuals with ID will be randomised to either the intervention group or control group (treatment as usual). Randomisation will occur after informed consent has been given and baseline assessments completed. Each arm will have 25 participants and be divided into five or more CST groups with up to five participants in each. Outcome assessments will include an assessment of cognitive functioning, adaptive functioning and quality of life in individuals with dementia and will also assess the feasibility of collecting the cost-effectiveness measures. A process evaluation will include qualitative interviews with participants, staff and carers to identify aspects of the intervention and study methods including adherence. Any direct quotations used from these interviews in the final publication will be anonymised.
Estimated total trial duration:	30 months
Planned trial sites:	North East London NHS Foundation Trust, East London NHS Foundation Trust, Camden & Islington NHS Foundation Trust, Central and North West London NHS Trust Foundation, London Community Health Care NHS Trust, and Barnet, Enfield & Haringey Mental Health Trust
Total number of participants planned:	50
Main inclusion/exclusion criteria:	Inclusion criteria 1. Mild or moderate Learning disabilities 2. ICD-10 diagnosis of mild or moderate dementia

Statistical methodology and analysis:	Exclusion criteria 1. Severe Learning disabilities 2. Severe dementia 3. Visual or hearing impairment that prevents participation As this is a feasibility study, we do not anticipate that there will be statistically significant differences in the outcome measures between the intervention and control groups. However, we will examine differences in the mean and standard deviation for the primary outcome (cognitive functioning) in order to calculate a sample size for a larger study.

3 Background and Rationale

Dementia is highly prevalent in people with Learning disabilities (LD) when compared to the general population, with research finding that it is almost five times higher (1) and people with Down's syndrome having a 90% risk of developing dementia in their later years (2). Dementia is therefore a significant cause of mortality (3). Cognitive Stimulation Therapy (CST) has a strong evidence base in terms of benefits for people with dementia in relation to cognitive function and quality of life (4). In the UK, NICE guidelines (5) recommend that everyone with mild to moderate dementia should be offered the opportunity to participate in a group CST programme. The evidence base however does not include studies on the effectiveness of CST in LD, and CST groups are therefore not routinely offered at present to those with ID, as there is no data that suggest it will be effective in this population. Research suggests that CST not only improves cognitive function and quality of life in people with dementia (6) but that it is also cost effective and has comparable efficacy to anti-dementia medication (7). The CST intervention is delivered in a group, typically 2 sessions a week of 45 minutes each over a period of 7 weeks (6). The intervention involves activities such as naming people and objects, word association, number and word games and discussion of current affairs. It uses a range of evidence-based methods such as errorless learning, reality orientation and multi-sensory stimulation (8,9). The benefits of CST could be linked to the activation of neuronal networks associated with cognition such as memory and language (10). It is thought the social interaction involved in the groups also helps in developing new semantic links which could also be associated with the improvement of language in the people who attend the groups (11).

Evidence from one pilot study investigating the effectiveness of group CST in improving cognition, adaptive functioning and quality of life compared to treatment as usual (12) in 25 participants with Down's syndrome found improvement in cognitive functioning at three months in the treatment group in comparison to the control group. Both groups showed an improvement in quality of life scores after three months in comparison to their pre-treatment scores, but this was not significantly different between the groups. The study showed that CST can be adapted for people with ID and that it would be valuable to explore this further in a population with comorbid ID and dementia. An additional feasibility study has also been conducted on individualised CST (iCST) by Ali et al. in 2019

(13). It explored CST being delivered on an individual basis by a family member or other informal care giver of the individual with ID and dementia. The study found that iCST was feasible and acceptable in this population; however a key limitation was that adherence to the treatment protocol was low by the carers. Group CST could therefore be considered a more optimal mode of delivering CST as the groups would instead be run by professionals in the Learning Disabilities teams.

The lack of evidence based treatments for dementia in people with ID is particularly concerning given the high incidence, prevalence, early onset and mortality in this group (1, 3, 14,). Currently there is only medication offered as a treatment for this group however the evidence for the effectiveness of this is also scarce and people with LD may be more prone to side effects (16). Whilst there is no or limited access to group CST for people with LD, in the general population it is the only evidence based non-pharmacological treatment available and has been proved to benefit cognition and quality of life and is cost effective (6,7). This health inequality urgently needs to be addressed, therefore it is necessary to explore how this evidence based psychosocial intervention might benefit people with LD and comorbid dementia. As iCST in the general population is not as established or evidence-based as group CST it appears that group CST should be explored for equity of treatments for those with LD.

3.1 Assessment and Management of Risk

There will be no invasive tests or procedures that will be included above standard care. All the assessments will be based on standardised questionnaires. The intervention is not invasive.

The table below summarise the risks and mitigations of all tests above standard care that are being performed in a table:

Intervention	Potential risk	Risk Management
Group Cognitive Stimulation Therapy	Distress to participants	If participants are distressed by activities, the session should be terminated and reassess with them their willingness to continue taking part in the study.
Administration of cognitive tests	Distress to participants	If participants are distressed, the session should be terminated.

4 Objectives

Primary:

To determine the feasibility of recruitment to a randomised controlled trial of group CST by examining the ability to recruit sufficient participants, number of eligible participants, willingness of clinicians to recruit participants, and willingness of participants to be randomised; drop-out rates, adherence and fidelity and acceptability of the intervention, appropriateness of the outcome measures and feasibility of collecting data for both clinical and economic evaluation.

1. Feasibility of recruitment will be ascertained from:

a. Adequate recruitment, defined as the number recruited to the trial. Go: At least 38 participants recruited to the trial, Review: 25-37 participants recruited to the trial, Stop: Less than 25 participants recruited to the trial.

b. Recruitment of eligible participants, defined as the percentage of participants recruited to the trial from those eligible. Go: At least 75% of eligible participants recruited, Review: 50-74% of eligible participants recruited, Stop: <50% of eligible participants recruited.

c. Eligibility, defined as the percentage of participants eligible from those approached. Go: At least 75% of approached participants are eligible, Review: 50-74% of approached participants are eligible, Stop: <50% of approached participants are eligible. Both the numerator and denominator are important here – if the denominator is too large it may be that the recruitment strategies need to be refined to streamline recruitment, the numerator being too small may indicate that the eligibility criteria need to be reviewed.

d. Willingness of participants to be randomised will be assessed by establishing the percentage of potential participants that refuse due to not wanting to be randomised and trial processes.

e. Retention, defined as the number of participants completing the trial from those recruited. Go: At least 75% of recruited participants complete the trial, Review: 50-74% of recruited participants complete the trial, Stop: <50% of recruited participants complete the trial. compare proportion of treatment and control group who return for follow up assessments.

2. Acceptability and adherence of CST will be ascertained from:

a. Overall attendance amongst the CST group participants. Confirmation of adequate attendance amongst sessions delivered. Go: 75% of all intervention sessions attended, Review: 50-74% of all sessions attended, Stop:< 50% of sessions attended.

b. Confirmation of adequate delivery of sessions. Go: 75% of all intervention sessions delivered, Review: 50-74% of all sessions delivered, Stop:<50% of sessions delivered.

c. Acceptability demonstrated through qualitative Interviews with 10 CST participants purposively sampled plus 10 carers and 10 group facilitators (two per NHS site).

Secondary:

1. To assess the fidelity of delivery of the groups by;

a. Recording the number of group CST sessions completed by each participant and level of engagement in the sessions measured using CST participation forms developed alongside the CST manual.

b. Exploring the quality of the intervention delivery according to the recordings and facilitators reflections on delivery fidelity. We will be using a validated CST adherence checklist in order to assess fidelity.

2. To assess the suitability of study outcome measures and determining the primary outcome measure for a future larger RCT:

a. Analysis of completion/ response rates of outcome measures with confirmation these can be collected from the participants.

Go (for each measure): At least 85% of participants fully complete the outcome measure at each time point, Review: 70 – 84% of participants fully complete the measure at each time point, Stop: <70% of participants fully complete the measure at each time point.

b. Examining whether the measures are sensitive to change as a result of the intervention will be established by the preliminary analysis proposed in the statistical analysis section.

3. Collecting resource use information.

Feasibility of collecting resource use data for generating cost information for use in an economic evaluation, including intervention costs. This uses a modified version of the Client Service Receipt Inventory (CSRI) to capture information on health and social care resource use relevant to this population and context, such that published unit costs from NHS Reference Costs and the Personal Social Services Research Unit (PSSRU) Health and Social Care unit costs could be applied to calculate costs in a future full RCT. The modified CSRI is being prepared by the health economist in collaboration with PPI collaborators, clinicians, and other trial team members, and includes information on primary and community health care, medications, routine and emergency hospital care and use of personal social services, provided either by the state or funded privately, as well as financial or related impacts on carers.

5 Trial design

The initial phase will involve the adaptation of the intervention and development of the CST manual for people with Learning disabilities and dementia, as well as the development of the CSRI resource use questionnaire.

1. **Recruitment of Participants in accordance with the inclusion and exclusion criteria & Baseline assessments**

   Participants will be recruited and selected in accordance with the inclusion and exclusion criteria. They will then be assessed prior to the groups with the outcome measures selected.

2. **Training of professionals in CST delivery**

Professionals in the participating trusts will be trained in the delivery of CST groups which will be provided by the research team. Support around reasonable adjustments to the materials in order for them to be delivered to the ability level of the participants would also be provided to potential group facilitators.

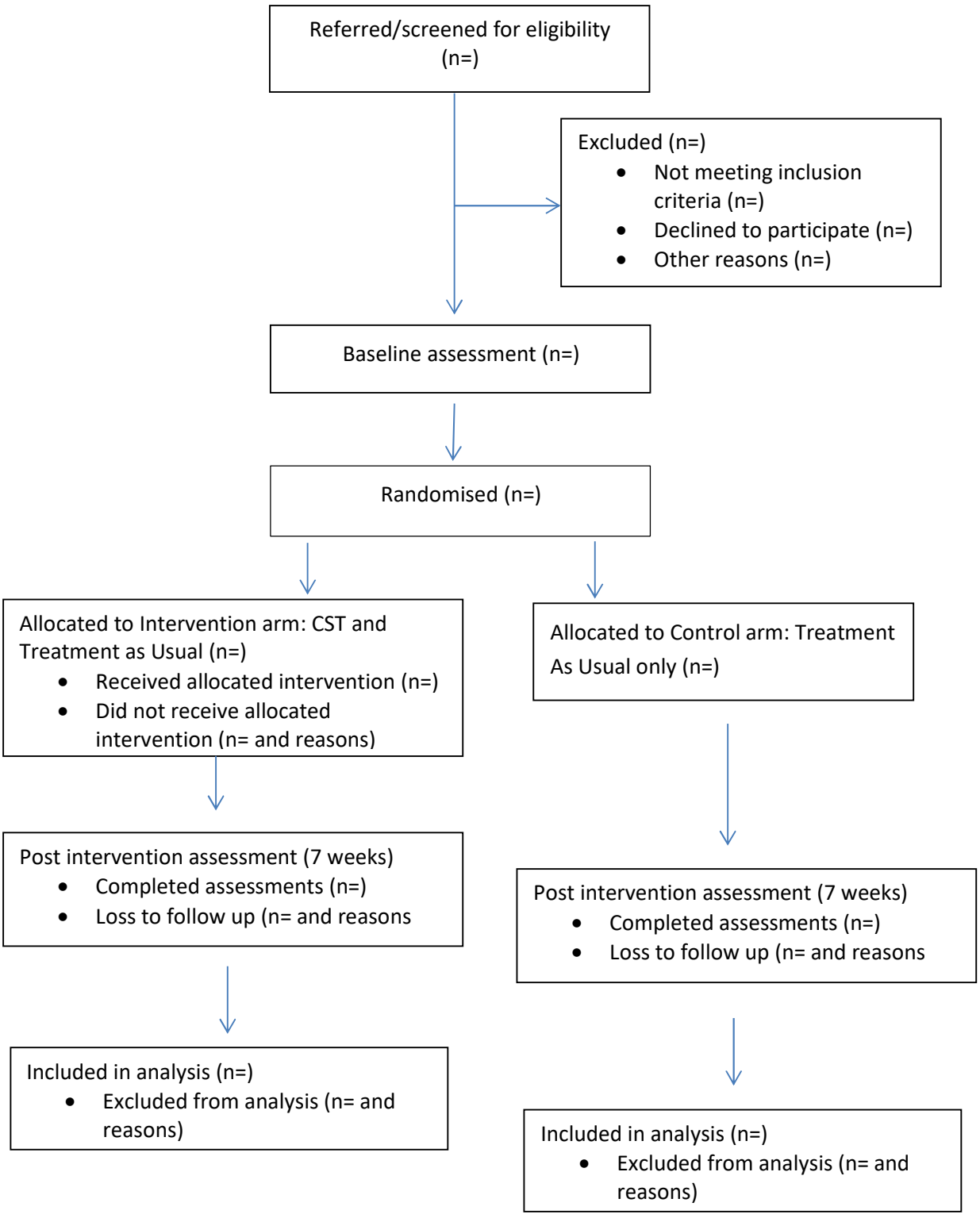
3. Feasibility Randomised Controlled Trial

This will be a single blind, pilot randomised controlled trial of CST delivered by professionals versus treatment as usual. Fifty participants will be randomised to either the intervention group or control group (treatment as usual). Randomisation will occur after baseline assessments are completed. Each arm will have 25 participants and they will be allocated to one CST group with up to five participants in each group.

The duration of the intervention will be 7 weeks. There will be assessments at baseline during the two weeks prior to randomisation, and at the end of the intervention after 8-9 weeks.

Please refer to figure 1 which shows the overall trial design.

Figure 1: Trial schematic diagram



6 Selection of Participants

6.1 Inclusion criteria

1. Premorbid mild or moderate Learning disabilities (based on clinical notes)
2. ICD-10 diagnosis of mild or moderate dementia
3. Is able to provide informed consent or where the participant lacks capacity, he/she has a personal consultee who has agreed to the participant taking part in the study.
4. To be able to communicate in English

6.2 Exclusion criteria

1. Severe Learning disabilities, preventing engagement in CST groups
2. Severe or late stage dementia
3. Has a visual impairment or hearing impairment that may interfere with the participant taking part
4. Has significant physical illness or disability preventing their participation
5. Has significant behavioural problems that could affect participation (e.g. aggressive behaviour)

Participants receiving anticholinesterase inhibitors as part of their usual treatment will not be excluded.

6.3 Recruitment

Participants will be recruited from community learning (Learning) disability teams based within the participating 5 NHS trusts including North East Foundation trust (NELFT), Central North West London Foundation Trust (CNWL), Camden and Islington (C&I), Barnet, Enfield and Haringey (BEH) and East London foundation trust (ELFT). The recruitment will be through the Learning Disabilities Teams in the first instance they will contact possible participants and gain consent to be contacted by the research team. The participants will likely be from multiple types of settings, including people who live in supported living, residential and family homes.

The Paticipants will have been diagnosed (or will be strongly suspected of having dementia) by a clinical psychologist and/or psychiatrist. Psychiatrists/psychologists will be asked to screen their case load for possible participants. Participants will then be approached by members of the multidisciplinary team who work closely with the participant and will discuss the study with the participant and their carer. If they are interested in taking part, they will be provided with an information sheet and their details will be passed on to the trial research assistant or CI. The research assistant will then contact the participant and their carer by phone and will arrange a meeting to

answer questions and to assess eligibility. If the participant (or a consulting carer) agree to taking part then informed consent will be obtained from the participant or consulting carer.

Participant recruitment at a site will only commence when the trial has:

1. Been confirmed by the Sponsor (or its delegated representative), and
2. Has received REC Favourable opinion and HRA Approval

6.4 Informed consent

It will be the responsibility of the research team to obtain written informed consent from each participant prior to participation in the trial, following adequate explanation of the aims, methods, anticipated benefits and potential hazards of the trial.

The person taking consent will be suitably qualified and experienced, and will have been delegated this duty by the PI of each of the sites on the Staff Signature and Delegation of Tasks.

"Adequate time" will be given for consideration by the participant before taking part. Consent will be sought at least 24 hours after being given the study documentation and obtained with a carer present. It must be recorded in the medical notes when the participant information sheet (PIS) has been given to the participant.

The Investigator or designee will explain that participants are under no obligation to enter the trial and that they can withdraw at any time during the trial, without having to give a reason.

No trial procedures will be conducted prior to the participant giving consent by signing the consent form. Consent will not denote enrolment into trial.

A copy of the signed Informed Consent form will be given to the participant. The original signed form will be retained in the trial file at site and a copy placed in the medical notes.

Where the participant loses capacity within the trial the PIS and consent form will be reviewed and updated if necessary throughout the trial (e.g. where new safety information becomes available) and participants will be re-consented as appropriate. If the participant is found to have lost capacity a personal consultee will be requested to provide a declaration. Where there is no personal consultee a nominated consultee will be requested.

Participants lacking capacity

The intervention will be taking place with participants who are able to provide informed consent at the time of consenting. However this might change through the duration of the study and therefore consent will be sought throughout the study period.

Capacity to take part in the research will be assessed by the delegated professional who will receive training on assessing capacity. He/she will determine whether the participant broadly understands the nature and purpose of the research and the risks and benefits of taking part or not taking part; whether the participant is able to retain the information; whether they can weigh up the pros and

cons of taking part in the research and whether they can communicate the decision (verbally or non verbally).

Where the participant found to be lacking capacity, we will follow the guidelines stipulated in the Mental Capacity Act (2005) in relation to including participants lacking capacity in research. A personal consultee will be consulted to consider the participant's beliefs and wishes about taking part in the study and will need to sign the declaration form before the participant is included in the study. If a personal consultee is not available, then we will consider approaching a nominated consultee (a member of the clinical team not directly involved in the research) to provide written agreement.

7 Product/Interventions

7.1 Name and description of intervention(s) under investigation

Group CST intervention

The intervention will comprise of 14 face to face sessions of CST based on a treatment manual. Each session will begin with discussion of the day, date, weather and location (5 mins) followed by discussion of events in the news or current issues (10 mins) and then the main activity (30 mins). The activities are based around a themed activity (e.g. life story, discussion of current affairs, being creative), which are designed to be mentally stimulating.

Two designated professionals from the Learning Disabilities team will be the group facilitators over a period of 7 weeks, 2 times per week. The groups will be run by professionals in the health team only, carers will not facilitate groups at any point. The activities will be tailored to the abilities and interests of the individuals with ID. Group facilitators will be asked to fill in the group monitoring sheet provided at the back of the CST manual. They will also receive advice and tips on how to adjust parts of the group programme to the level of ability of participants with ID and dementia i.e. using visual cues and replacing words with pictures where possible.

The intervention group will continue to have access to their usual care, which includes input from health and social care professionals, anti-dementia medication and their usual day activities.

Control group

The control group will have access to their usual care only for the duration of the trial. At the end of their participation in the study, once follow up data has been collected, the professionals can offer the groups to those who were in the control arm of the study. They will also continue to have access to support and care from their community learning disability service. To avoid disparity in care we will ensure that only one person per residential or supported living home is recruited. We will inform the participants that they may not receive the intervention if they are in the control group.

7.2 Storage and handling of drug at site (if applicable)

Not applicable

7.3 Accountability of drug (if applicable)

Not applicable

7.4 Concomitant medication (if applicable)

The participants will be permitted to take any medication that they usually take, including medication that may enhance cognition (e.g. acetyl cholinesterase inhibitors). These will be recorded carefully at baseline and follow up.

Concomitant medications will be recorded in the participant's medical records and in the trial's CRF.

7.5 Dosages, modifications and method of administration (if applicable)

Not applicable as the research team will not be administering any drugs.

8 Trial procedures

8.1 Pre-intervention assessments

All the participants with dementia and Learning disability will be screened for the presence of dementia based on ICD-10 criteria by the research team. This will be assessed using the criteria from the CAMDEX-DS. If the participants meet the criteria, they will complete the following baseline assessments (at home) prior to randomisation we will also collect demographic information of the participant. This will be done face to face with the carer present and following the outcome measures guideline instructions. The researcher will take with the hard copies of the assessments and enter data in the online system within 48 hours.

The outcome measures will be completed before the randomisation process and during week 8 and 9, after the intervention. The outcome measures have been described in the table below:

Type of measure	Name of measure	Comments	Rated by
Cognition	Severe Impairment Battery (SIB)	Originally developed for people with severe dementia in the general population, it has been used to assess dementia in people	Administered by researcher to individual with dementia (Direct assessment)

		with ID. Takes approx. 20 mins to complete. Assess 6 subscales: orientation, attention, language, memory, visuo-spatial ability, construction. Evidence suggests that it has good test-retest and concurrent validity in people with ID.	
Cognition	Dementia Questionnaire for people with Learning Disabilities (DLD)	Widely used in clinical practice and for measuring change in symptoms over time. Eight subscales split into two categories: Cognitive Score and Social Score Reference:	Completed by carer
Quality of Life	Quality of Life in Alzheimer's Disease (QOL-AD)- Proxy version	13 item scale covering physical health, mood, family life and functioning. Not developed for use in ID population but was used in iCST study and found to have a large effect size	by carers
Symptoms of depression	Glasgow Depression Scale for People with Learning Disability (GDS-LD) proxy version	16 item scale. Good internal consistency and inter-rater reliability.	Rated by carer
Health related Quality of Life	EQ-5D-5L	The EQ-5D-5L is a 5-item health utility instrument that captures participants' self-rated status in five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression; according to five levels: no problems, slight problems, moderate problems, severe problems and extreme problems. There is also an accompanying visual analogue scale (0-100) that is completed at the same time for valid use of the questionnaire. The responses to the five dimensions are	Rated by individual

		transformed into a single utility score using an algorithm, and the utility score is scaled with 1=perfect health and 0 being equivalent to dead. The utility score can be used to calculate quality-adjusted life-years, if the EQ-5D-5L is captured across more than one timepoint.	
Health related Quality of life	EQ-5D-5L- Proxy version 1	This is the same questionnaire as above, and the carers will be asked to complete it by proxy for the dementia patient.	Rated by carer (carer reports person's QoL based on their own opinion)
Health Service Utilisation	Client Services Receipt Inventory (modified version)	This questionnaire captures information on health and social care resource use, such as primary and community health care, medications, routine and emergency hospital care and use of personal social services, provided either by the state or funded privately, as well as financial or related impacts on carers. Costs will be calculated by applying standard unit costs to the information gathered via the CSRI.	Completed by carer

All pre-treatment procedures will be carried out as specified in the schedule of assessments.

8.2 Randomisation Procedures

Randomisation will occur after eligibility, consent and baseline assessments have been carried out by the blinded research assistant. Randomisation will be undertaken by the coordinating trials unit (NWORTH) using a dynamic adaptive randomisation algorithm via a secure online interface. An unblinded member of the team will enter necessary details into the web based randomisation system. This system will randomly allocate the participant to either the intervention or control arm. Randomisation will be stratified for recruited NHS Trust site/centre. Participants will be randomly allocated to intervention group or control group and informed of group allocation by an unblinded member of the research team. Although participants cannot be blinded to their allocated group, the research assistant administering the questionnaires will be blinded to the allocation group. Due to the risk of carers revealing the allocation group, participants and their carers will be reminded before the follow-up assessments not to divulge this information. At the end of the study, we will assess researcher blindness by asking them to guess the allocated group.

8.3 Intervention procedures

Group Cognitive Stimulation Therapy is a group intervention for people with mild to moderate dementia designed following extensive evaluation of the available research and is an evidence-based treatment. The programme consists of fourteen 45-minute sessions which are run twice weekly over 7 weeks. Each session incorporates use of a reality orientation board, displaying both personal and orientation information, including the group name (as chosen by participants). The guiding principles of CST involve using new ideas, thoughts and associations; using orientation (but sensitively and implicitly); a focus on opinions rather than facts; using reminiscence as an aid to the here-and now; providing triggers to aid recall; creation of continuity and consistency between sessions; focus on implicit (rather than explicit) learning; stimulating language; stimulating executive functioning and being person-centred - (treating people as unique individuals with their own personality and preferences). The CST programme aims to create an environment where people have fun, learn and where they strengthen their abilities and relationships among the group members, thus maintaining their social and cognitive skills at their optimum ability.

As part of a NELFT service evaluation, CST was delivered to a group of patients with comorbid ID and dementia including a reduced number of group participants with a maximum of five people in each group. The activities within sessions used visual aids to convey information about time and place, “easy read” newspaper articles to discuss current events, and simplified activities within each theme so that they were accessible to people with ID. Within the original structure of CST, sessions are allowed to be flexible in order for the activities to be adapted to different interests as well as different levels of cognitive function.

8.5 Samples (if applicable)

Not applicable

8.6 Discontinuation/withdrawal of participants

A participant may be withdrawn from trial whenever continued participation is no longer in the participant’s best interests, but the reasons for doing so should be recorded. Reasons for discontinuing the trial may include:

- disease progression whilst in trial
- Chronic current illness
- patients withdrawing consent or Personal/Nominated Consultees withdrawing assent for participants lacking capacity

The decision of a participant to withdraw from treatment will be recorded in the CRF and medical notes. If a participant withdraws from the intervention, they will be asked to continue to provide follow up data. Their decisions regarding withdrawal from the intervention and withdrawal from follow-up will be recorded in their medical notes and in the trial CRF, along with any reasons that they have shared.

8.7 Definition of End of Trial

The expected duration of the trial is 30 months from recruitment of the first participant.

8 Recording and reporting of adverse events

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or trial participant, which does not necessarily have a causal relationship with the intervention involved.
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*, • requires hospitalisation or prolongation of existing hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect.
* A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

9.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality, seriousness and expectedness as described and outlined in the Sponsor SOPs documents stored on the NELFT R&D shared drive.

9.2.1 Severity

The generic categories below are given for use as a guide.

Category	Definition
Mild	The adverse event does not interfere with the participant's daily routine, and does not require further intervention; it causes slight discomfort
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further intervention, but is not damaging to health; it causes moderate discomfort
Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health

9.2.2 Causality

The assessment of relationship of adverse events to the intervention is a clinical decision based on all available information at the time of the completion of the case report form.

If a differentiated causality assessment which includes other factors in the trial is deemed appropriate, please add/amend the following wording to specify:

It is of particular importance in this trial to capture events related to the procedure (Cognitive Stimulation Therapy) (refer to section 9.17 for reporting requirements). The assessment of relationship of an adverse event to this/these additional safety issue(s) will also be carried out as part of the trial.

The differentiated causality assessments will be captured in the trial specific CRF or SAE form (amend as required).

The following categories will be used to define the causality of the adverse event:

Category	**Definition**
Definitely:	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably:	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely
Possibly	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of the trial intervention). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial intervention). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatments).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

9.2.3 Expectedness

Category	Definition

Expected	An adverse event which is consistent with the information about the intervention listed in the SPC, manual of Operation (amend as appropriate) **or clearly defined in this protocol.**
Unexpected	An adverse event which is not consistent with the information about the intervention listed in the SPC, manual of Operation (amend as appropriate)* **or clearly defined in this protocol.**

* This includes listed events that are more frequently reported or more severe than previously reported.

There are no known adverse effects of Cognitive Stimulation Therapy. However, taking part may possibly cause distress/ inconvenience for some participants with dementia

9.3 Recording adverse events

All adverse events will be recorded with clinical symptoms and accompanied with a simple, brief description of the event, including dates as appropriate.

All adverse events will be recorded in the CRF until the participant completes the trial.

9.4 Procedures for recording and reporting Serious Adverse Events

All serious adverse events will be recorded in the participant records hold in the Trust and the CRF, and the sponsor's AE log. The AE log of SAEs will be reported to the sponsor at least once or twice per year.

All SAEs (except those specified in section 9.5 as not requiring reporting to the Sponsor) must be recorded on a serious adverse event (SAE) form. The CI/PI or designated individual will complete the sponsor's SAE form and the form will be preferably emailed to the Sponsor within 5 working days of becoming aware of the event. The Chief or Principal Investigator will respond to any SAE queries raised by the sponsor as soon as possible.

Where the event is unexpected and thought to be related to the intervention, this must be reported by the Investigator to the Health Research Authority within 15 days.

9.5 Serious Adverse Events that do not require reporting (if applicable)

Not applicable

9.6 Unblinding (if applicable)

This is not relevant as the participants will be aware of the whether or not they are receiving the intervention. The research assistant administering the questionnaires will be blind to the treatment group.

9.7 Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI/ PI shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures.

9.8 Notification of reportable protocol violations

A reportable protocol violation is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

The sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase.

9.9 Reporting incidents involving a medical device(s) (if applicable)

Not applicable

9.10 Trust Incidents and Near Misses

An incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.
b. It is contrary to specified or expected standard of patient care or service.
c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d. It puts the Trust in an adverse position with potential loss of reputation.
e. It puts Trust property or assets in an adverse position or at risk.

Incidents and near misses must be reported to the Trust through DATIX as soon as the individual becomes aware of them.
A reportable incident is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a) It is an accident or other incident which results in injury or ill health.
b) It is contrary to specified or expected standard of patient care or service.
c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d) It puts the Trust in an adverse position with potential loss of reputation.
e) It puts Trust property or assets in an adverse position or at risk of loss or damage.

10 Data management

10.1 Confidentiality

All data will be handled in accordance with the GDPR guidelines.

The Case Report Forms (CRFs) will not bear the participant's name or other personal identifiable data. The participant's initials, date of birth and trial identification number, will be used for identification and this will be clearly explained to the patient in the Patient information sheet. Patient consent for this will be sought.

10.2 Data collection tools and source document identification

Data will be collected from sites on trial specific case report forms (CRFs). The data will be anonymous and entered into the electronic data capture system, so that data can be extracted for statistical analysis.

Source data are contained in source documents and must be accurately transcribed on to the CRF. Examples of source documents are medical records which include laboratory and other clinical reports etc.

A source document list will be implemented prior to the start of the trial to identify:

- which data is to be recorded directly onto the CRF;
- which data is recorded firstly into source documents, such as medical notes, and then transcribed into the CRF; and
- which data is not to be recorded in the CRF but only recorded in source documents, e.g. participant questionnaires.

It is the responsibility of the investigator to ensure the accuracy of all data entered in the CRFs. The delegation log will identify all those personnel with responsibilities for data collection and handling, including those who have access to the trial database.

10.3 Completing Case Report Forms

All CRFs must be completed and signed by staff that are listed on the site staff delegation log and authorised by the CI/ PI to perform this duty. The CI/PI is responsible for the accuracy of all data reported in the CRF.

Once completed data from the CRFs will be entered into the electronic data capture system. The data can then be downloaded for data cleaning and statistical analysis. The original copies must remain at the sponsor site and securely stored. Source data verification of a CRF page should be completed and all data queries answered prior to submission where possible.

10.4 Data handling

In the study, questionnaires (see section on pre-assessment and assessment measures) will be collected from patients in accordance with the patient consent form, patient information sheet and section 8 of this protocol.

The questionnaires will be appropriately kept at the Research and Development Department at North East London NHS Foundation Trust and the employed research assistant supervised by NELFT study PI will act as the data controller of such data for the study. Data will be entered into a database hosted on RedCap by the research assistant and may be downloaded by NWORTH electronically for data cleaning and statistical analysis. Any other data transferred to NWORTH will be encrypted, password protected and contain no identifiable data. A data management plan will be developed to describe procedures for data storage and data cleaning.

11 Statistical Considerations

11.1 Statistical analysis

Baseline characteristics will be summarized for all participants, the intervention group and control groups separately. Participants' uptake of and adherence to the intervention, as well as follow-up rates, will be summarized and presented as percentages.

Although determining differences in clinical outcomes between the arms is not the primary purpose of this trial, comparisons will be undertaken to investigate the feasibility of studying these outcomes and to calculate estimates for the likely effect sizes and 95% confidence intervals. As recommended in guidelines for good practice for the analysis of pilot studies, the focus of the results will be on the estimates of the treatment effects rather than statistical significance and as such no hypothesis testing will be undertaken. Differences between the two comparison groups will be presented in the form of an unadjusted mean difference for continuous outcomes, and an odds ratio for binary outcomes, with

their associated 95% confidence intervals. Despite the individual randomisation there is group based treatment and therefore consideration will also be made in regard to estimation of the potential intra-cluster correlation (ICC) coefficient. The estimation of the likely ICC will be able to guide the sample size of a future trial.

11.2 Sample size calculation

This is a feasibility study with no formal power calculation. Instead, a sufficient number of participants need to be recruited in order to determine the attrition and recruitment rates and how these are related to feasibility for a full scale RCT. By setting our target sample size at 50 we will achieve adequate precision around our expected retention rate of 75% (95% confidence interval of 62-86%) to determine the feasibility going forward. Based on our previous study data we are anticipating we will have to screen a maximum of 70 people to reach our sample size.

There is no available data on the use of Cognitive Stimulation Therapy in the treatment of dementia in people with Learning disability. This sample should also provide adequate precision using a confidence interval approach which considers the likelihood of a future definitive study finding a relevant effect size.

11.3 Planned recruitment rate

We will be recruiting for ten to fifteen months. We estimate that we will recruit four eligible participants each month from at least seven learning disability services in London. If recruitment is anticipated to be slow, we will recruit other centres if necessary.

12 Health Economics

12.1 Health economic analysis

As this is a feasibility study, the focus will be on the feasibility of collecting data that would be used in a future cost-effectiveness (CEA) alongside a larger future RCT. The aim of that future CEA would be to report the incremental cost per quality-adjusted life-year gained on using group CST compared to treatment as usual, over the time period of the study, from the perspective of the NHS and Personal Social Services.

12.2 Quality of life (QOL) and quality-adjusted life years (QALYs)

The EQ-5D-5L is administered to all participants at baseline and at follow-up, to allow reporting of different domains of the participant's health-related quality of life (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and to see how this has changed in each of the two randomised groups, and to allow utility weights (also called QOL scores or values) to be

calculated from the responses to the EQ-5D-5L using standard algorithms. These QOL values, calculated from the EQ-5D-5L responses captured from participants at baseline and follow-up, are then used to calculate quality-adjusted life-years (QALYs) for participants over the time horizon of the study, using area under the curve methods. QALYs are calculated adjusting for baseline QOL values.

QALYs are the outcome preferred for use in cost-effectiveness analysis by the National Institute for Health and Care Excellence (NICE) when combined together with information on costs. The five questions covering the five domains listed above are followed by a visual analogue score on the second page of the questionnaire, which is not used in health economic analysis but is required to be included for valid administration of the questionnaire.

The feasibility study outcomes here will assess proportions of participants who return completed EQ-5D-5L questionnaires (focusing on the 5 items on the first page and considering the VAS responses separately) at the two timepoints.

12.3 Resource use and costs

Besides QALYs, the CEA alongside the future full RCT would require information on costs to the NHS and Personal Social Services (NHS+PSS) of using the group CST intervention and using treatment as usual. Costs would include cost of the intervention in that arm, costs of treatment as usual in both arms, and any other treatment pathway costs, i.e. primary and community health care, medications, routine and emergency hospital care and use of personal social services, provided either by the state or funded privately, as well as financial or related impacts on carers. We would include privately funded care, and impacts on carers, as this is likely to be important in this group, although it would not be included in the base case analysis in the future CEA as it is outside the perspective of the NHS+PSS. We are also collecting baseline costs (i.e. CSRI administered at baseline and carers asked for the participant's preceding 8 weeks of resource use) so that these can be adjusted for in the future analysis.

We will firstly develop an appropriately modified CSRI questionnaire, with input from PPI, clinicians, and others in the trial team, and then use this in our feasibility study to assess the feasibility of collecting resource use data for generating cost information for use in a future RCT in this population and context. Our patient and public involvement collaborators, along with clinicians and other members of the study team, will be involved in modifying the CSRI questionnaire for use in this feasibility study, in terms of tailoring the content and language to make sure it is suitable and that we can try and collect relevant data without over-burdening participants or carers.

The feasibility study outcomes here will assess rates of completion of the different parts of this questionnaire at the two timepoints, and what changes might need to be made to the questionnaire on the basis of the feasibility study outcomes and qualitative feedback, before using an updated and refined version of it in a future larger study.

13 Record keeping and archiving

At the end of the trial, all essential documentation will be archived securely by the CI for a minimum of 20 years from the declaration of end of trial.

Essential documents are those which enable both the conduct of the trial and the quality of the data produced to be evaluated and show whether the site complied with all applicable regulatory requirements.

The sponsor will notify sites when trial documentation can be archived. All archived documents must continue to be available for inspection by appropriate authorities upon request.

14 Oversight Committees

13.1 Trial Management Group (TMG)

The TMG will include the Chief Investigator and trial staff. The TMG will be responsible for overseeing the trial. The group will meet regularly (four times a year) and will send updates to Trust PIs.

The TMG will review recruitment figures, SAEs and substantial amendments to the protocol prior to submission to the REC. All PIs will be kept informed of substantial amendments through their nominated responsible individuals.

15 Ethical requirements and patient and public involvement

Ethics

The sponsor will ensure that the trial protocol, participant information sheet, consent form, GP letter and submitted supporting documents have been approved by the appropriate research ethics committee, prior to any participant recruitment. The protocol, all other supporting documents including and agreed amendments, will be documented and submitted for ethical and HRA approval. Amendments will not be implemented prior to receipt of the required approval(s).

Before any NHS site may be opened to recruit participants, the Chief Investigator/Principal Investigator must obtain HRA approval and all subsequent amendments must be submitted for HRA approval. This does not affect the individual clinician's responsibility to take immediate action if thought necessary to protect the health and interest of individual participants (see section 9.6 for reporting urgent safety measures).

An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended. The chief investigator will prepare the APR.

Within 90 days after the end of the trial, the CI/Sponsor will ensure that the main REC is notified that the trial has finished. If the trial is terminated prematurely, those reports will be made within 15 days after the end of the trial.

The CI will supply the Sponsor with a summary report of the trial, which will then be submitted to the REC within 1 year after the end of the trial.

Patient and public involvement (PPI)

Service users/patients with Learning disability and their carers will be involved in adapting the activities within the Cognitive Stimulation Therapy manual, in order to produce an adapted version that will be suitable for individuals with Learning disability and dementia. They will also be involved in modifying the CSRI questionnaire for use in this study. The study PPI lead will be involved in all study meetings to help design and plan the study, and PPI will be consulted throughout for the development of dissemination of study findings.

16 Monitoring

The study will be conducted according to Good Clinical Practice (GCP) Guidelines.

Research Capacity: The Sponsor will ensure that appropriate checks are made with each Trust/Organisation to ensure they have the capacity to accommodate the research. Each Trust/Organisation will be supplied with an Investigator Site File (ISF) and the PI will be responsible for overseeing the maintenance of this file in accordance with the SOP provided.

Monitoring: The Sponsor accepts responsibility for monitoring the trial; (i) “Ensuring the rights and well-being of the participants are protected; (ii) checking that the reported trial data are accurate, complete, and verifiable from source documents; and (iii) that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s)” (ICH-GCP 5.18.1).

The study team will work closely with the monitor to determine the monitoring requirements for each Trust/Organisation involved in the trial and set out a schedule for monitoring accordingly. This schedule will follow the

NELFT minimum monitoring requirements which are; (i) study and site(s) monitoring as part of study and site(s) initiation before the trial commences, (ii) “First recruits monitoring” to take place upon recruitment of an agreed number of participants; (iii) study and site(s) will be monitored at least annually during the trial; and (iv) study and site(s) will be monitored as part of study and site(s) closure. Specific processes will be outlined in a Sponsor SOP supplied to trial sites.

During the study all sites will be required to follow the Sponsor SOP for research incidents and protocol related deviations and a study specific SOP for the reporting and recording of serious adverse events. The Sponsor accepts responsibility for closing the study at each site and archiving study information. All research and clinical staff involved in the research activities will be trained, supervised and supported.

Recruitment Monitoring: Recruitment monitoring will take place during the study via teleconference. Meetings will be chaired by the Chief Investigator and minutes recorded and disseminated to sites. Site PIs and their researchers will be welcome to attend and will be given the opportunity to discuss their recruitment figures, challenges and successes. Frequent monitoring will give teams the opportunity to troubleshoot queries as they arise. The degree of monitoring will be proportionate to the risks associated with the trial. The degree of monitoring will be proportionate to the risks associated with the trial.

A trial specific oversight and monitoring plan will be established for studies. The trial will be monitored in accordance with the agreed plan.

17 Finance

The study is being funded by NIHR RfPB funding ID NIHR201934. They have agreed to provide a funding of £245,697.00 subject to obtaining ethical approval.

There are no conflicts of interest to declare.

18 Insurance

NELFT holds insurance against claims from participants for injury caused by their participation in the trial. Participants may be able to claim compensation if they can prove that NELFT has been negligent.

19 Publication policy

We will agree a publication strategy at the outset including authorship on papers. All proposed publications will be open access in accordance with NIHR guidance.

20 Intellectual property

All background intellectual property rights (including licences) and know-how used in connection with the study shall remain the property of the party introducing the same and the exercise of such rights for purposes of the study shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol and in the results arising directly from the study, but excluding all improvements thereto or clinical procedures developed or used by each participating site, shall belong to NELFT.

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